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10/600,361

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Jean-Marie Andrieu

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EXAMINER

LE, EMILY M

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/600,361 | Applicant(s) ANDRIEU ET AL. | |
| | Examiner EMILY M. LE | Art Unit 1648 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10/16/08+12/11/08.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 44 and 52-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 44 and 52-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 10/16/08 and 11/18/08 has been entered.

Status of Claims

2. Claims 1-43, 45-51 are cancelled. Claims 44 and 52-56 are pending and under examination.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Belardelli et al.¹

The claims are directed to a composition comprising dendritic cells pulsed with an inactivated human immunodeficiency virus (HIV), wherein the dendritic cells are obtained from a monocyte by plastic-adherence followed by culture with GM-CSF and

¹ Belardelli et al. U.S. PreGrant Patent No. 2003/0092177 A1, filed April 27, 2001.

Art Unit: 1648

IL-4 and a pharmaceutically acceptable carrier, requires that the virus be autologous and wherein the virus is chemically inactivated by 2,2'-dithiopyridine. Additionally, the claims require that the virus be isolated from the blood tissue of the patient, and that composition be obtained by isolating peripheral blood mononuclear cells from whole blood, subjecting the peripheral blood mononuclear cells to plastic adherence, culturing the adherent cells with GM-CSF and IL-4 to obtain the dendritic cells, adding to 2,2'-dithiopyridine-inactivated virus to the dendritic cells and culturing the cells.

Belardelli et al. teaches composition comprising dendritic cells pulsed with an inactivated human immunodeficiency virus (HIV) and a pharmaceutically acceptable carrier. [Paragraphs 0066-0067 and 0071, in particular.] The dendritic cells used by Belardelli et al. were obtained from a monocyte by plastic-adherence followed by culture with GM-CSF and IL-4. Belardelli et al. uses AT-2, 2,2'-dithiopyridine, to chemically inactivate the virus. And Belardelli et al. uses autologous dendritic cells.

While the dendritic cells used by Belardelli et al. are autologous, it is not readily apparent if the virus used by Belardelli et al. is also autologous. It should be noted that Belardelli et al. uses the cells as an adjuvant, and the inactivated virus as an immunogen/antigen.

However, due to the many variability in the many type of HIV isolates and the ability of the virus to mutate, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to use autologous HIV. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to induce an immune response against the specific HIV isolate infecting the

Art Unit: 1648

subject. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the use of autologous antigens is routinely practiced in the art.

It is noted that the claims require the composition to expands *in vivo* expression of virus-specific CD8+ T cells, and said virus-specific CD8+ cells kill HIV-infected cells; however, MPEP § 2112 [R-3] (I) provides: [T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In *re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." *Id.*

In the instant case, while it may be true that Applicant discovers that the claimed composition expands *in vivo* expression of virus-specific CD8+ T cells, and said virus-specific CD8+ cells kill HIV-infected cells; however, this discovery does not make the composition patentable over the composition of Belardelli et al. Belardelli et al. teaches

a composition that is the same as instantly claimed. The composition of Belardelli et al. is the claimed composition. Hence, Belardelli et al. does not need to teach that the composition expands *in vivo* expression of virus-specific CD8⁺ T cells, and said virus-specific CD8⁺ cells kill HIV-infected cells to anticipate the claimed invention. The composition of Belardelli et al. would have the same properties or functions recognized by Applicant.

Regarding the process by which the claimed product is made, it should be noted that even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” MPEP 2113, *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

In response to the previous rejection of the claims over Belardelli et al., Applicant argues that Belardelli et al. teaches away from the use of GM-CSF and IL-4 to obtain the dendritic cells. Applicant also argues that the reference does not teach the use of autologous HIV virus isolated from blood tissue of a patient. Applicant additionally asserts that the rejection is improper because it is not based on any fact on the record. Applicant submits the Gougeon declaration for consideration. Gougeon declaration asserts that in view of Richman², one of ordinary skill in the art would have a

² Richman et al. Rapid evolution of the neutralizing antibody response to HIV type 1 infection. PNAS, April 2003, Vol. 100, No. 7, 4144-4149.

reduced "expectation of successfully modifying Belardelli in the way the Official Action proposes" because Richman noted difficulties associated with the experimental use of autologous HIV. The Gougeon declaration also states that the lack of reasonable expectation of successfully modifying Belardelli by using autologous HIV is underscored by the failure of others, Garcia et al.³ Gougeon asserts that based on Garcia et al., who teaches that heat-inactivated vaccine was capable of eliciting "weak and transient" cellular immune responses and that based on such, it could be argued the vaccine did not elicit specific anti-HIV-1 immune response at all., one of ordinary skill in the art would not reasonable expect that the use of inactivated HIV to create a dendritic cell based vaccine would be successful in expanding the expression of CD8+ cells. Lastly, Applicant argues that the rejection improperly relies on an inherency type argument. Lastly, Applicant argues that the rejection improperly relies on an inherency type argument.

Applicant's arguments have been considered, however, it is not found persuasive. MPEP 2123 (II) provides, "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). In the instant case, while Belardelli et al. does teach of several methods of generating production of dendritic cells, including one that is a preferred embodiment of Belardelli et al., however, it should be noted that Belardelli et al. does not teach away from the

³ Garcia et al. Therapeutic immunization with dendritic cells loaded with heat-inactivated autologous HIV-1 in patients with chronic HIV-1 infection. J. Infect. Dis. May 2005, Vol. 191, No. 10, 1680-1685.

use of GM-CSF and IL-4 for the reference does not criticize, discredit or otherwise discourage the use of such dendritic cells production method.

As recognized in the office action, the reference does not teach the use of autologous cells. Had the reference teaches such, the Office would have cited the reference in an anticipatory rejection instead of an obviousness rejection. To compensate for the noted deficiency in the prior art, the Office clearly and properly sets forth an obviousness rejection. Contrary to Applicant's assertion, an obviousness rejection need not to be limited to the teachings expressed therein, obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found **either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.** See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The Gougeon declaration, which has been considered, however, it is not sufficient to overcome the rejection. Regarding the assertion that "one of ordinary skill in the art would have a reduced "expectation of successfully modifying Belardelli in the way the Official Action proposes" in view of the teachings of Richman et al., Applicant is reminded that the standard is reasonable expectation of success and not absolute success. Additionally, it should be noted that the difficulties of Richman et al. is not directed at the making of autologous HIV. Rather the difficulties are directed at the measurement of neutralizing antibody responses. While it is noted that Richman et al. mentions that technical challenges are associated with the preparation of autologous

Art Unit: 1648

virus that are typically obtained from peripheral blood mononuclear cells, however, as noted above, the standard is reasonable expectation of success. In the instant case, Richman et al. failed to demonstrate that one of ordinary skill would not be able to reasonable expect success in obtaining autologous HIV for use with the composition of Belardelli et al.

As for the Garcia et al. reference, which has been considered, however, it is not sufficient to demonstrate a lack of reasonable expectation of success. While Garcia et al. does note that that due to the weak and transient cellular immune response, it could be argued that the vaccine did not elicit specific anti-HIV-1 immune response at all, however, Garcia et al. does note that it could also be such conclusion could be argued against, which Garcia et al. details on page 1684. And, contrary to Applicant's assertion that one of ordinary skill in the art would not reasonably expect to elicit CD8+ T cell response, Garcia et al. was able to elicit HIV-1 specific CD8+ T cell response with the administration of a composition comprising autologous dendritic cells pulsed with inactivated whole autologous HIV-1 virus.

Regarding Applicant's assertion that the Office has improperly relied on an inherency type argument, which has been considered, however, it is not found persuasive. The rejection itself is not based on inherency. Rather inherency was used to evidence that the composition of Belardelli et al. also is capable of inducing CD8+ T cell response for it comprises the inactivated HIV virus as the antigen and dendritic cells to present the antigen to both helper and cytotoxic T cells required by the claimed invention. Belardelli et al. discloses that his composition induces CD8+ T cell.

5. Claims 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belardelli et al., as applied above to claim 44, in view of Lu et al.⁴

In response to the rejection, Applicant argues that the teachings of Lu et al. do not cure the deficiencies noted of Belardelli et al.

The Applicant's noted deficiencies of Belardelli et al. is detailed and addressed in paragraph 3 of this office action.

The claims require the composition to further comprise an adjuvant. The adjuvant is later limited to a protease inhibitor by claim 53, which depends on claim 52. The protease inhibitor is later limited indinavir by claim 54, which depends on claim 53. Claim 55, which depends on claim 54, later requires that the composition comprise a non-antiviral concentration of indinavir. And claim 56 limits the non-antiviral concentration to 10 nM.

The significance of Belardelli et al., as applied to claim 43, is provided above.

The composition of Belardelli et al. does not further comprise indinavir. However, Lu et al. teaches that indinavir direct up-regulate proliferation and down regulate apoptosis of T cells. [Paragraph bridging pages 247-248.]

Thus, would have been prima facie obvious for one of ordinary skill in the art to combine the teachings of Belardelli et al. and Lu et al. One of ordinary skill in the art would have been motivated to do so to optimize CTL response against HIV infection. One of ordinary skill in the art at the time the invention was made would have had a

⁴ Lu et al. HIV protease inhibitors restore impaired T-cell proliferative response in vivo and in vitro: a viral-suppression-independent mechanism. Blood, Jul 2000; Vol. 96, 250 - 258.

Art Unit: 1648

reasonable expectation of success for doing so because the determination of a workable or optimal range is routinely practiced in the art.

It is recognized that claims require the composition to contain non-antiviral concentration of indinavir, specifically 10 nM. In the instant, Lu et al. teaches that the extent in which indinavir up-regulate proliferation and down regulate apoptosis of T cells varies at different concentrations of indinavir. Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use any concentrations of indinavir, particularly since Lu et al. establishes that indinavir at various concentrations, ranging from .1nM to 1000 nM, stimulates direct up-regulate proliferation and down regulate apoptosis of T cells. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to determine the optimum concentration to optimize the proliferation of T cells. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the determination of workable ranges or optimal value is routine practiced in the art.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

Art Unit: 1648

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. The provisional obviousness-type double patenting rejection(s) of the claims over copending patent application(s) is withdrawn in view of the elected subject matter in the copending patent application.

Conclusion

8. No claim is allowed.

Art Unit: 1648

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to EMILY M. LE whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/EMILY M LE/
Primary Examiner, Art Unit 1648

/E. M. L./